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(21) International Application Number: PCT/IB99/00866 (22) International Filing Date: 14 May 1999 (14.05.99) (30) Priority Data: 10/141379 22 May 1998 (22.05.98) JP (71) Applicant (for all designated States except US): HOECHST MARION ROUSSEL LTD. [JP/JP]; 17-51, Akasaka 2-chome, Minato-ku, Tokyo 107-8465 (JP). (72) Inventors; and (75) Inventors/Applicants (for US only): KAWAI, Shinji [JP/FR]; 416, rue Emile Dubois, F-75014 Paris (FR); KIMURA, Michio [JP/JP]; 9-8-304, Tsurugadai, Chigasaki-shi, Kanagawa 253-0003 (JP); MURAKI, Yoshifumi [JP/JP]; Hoechst Marion Roussel Ltd., Product Realization Dept., 17-51, Akasaka 2-chome, Minato-ku, Tokyo 107-8465 (JP); KATSUURA, Mieko [JP/JP]; 2-14-2-106 Sakae-cho, Higashimurayama-shi, Tokyo 189-0013 (JP). (74) Agent: VIEILLEFOSSE, Jean-Claude; Hoechst Marion Rous- sel, 102, route de Noisy, F-93235 Romainville Cedex (FR).		(81) Designated States: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report.	

(54) Title: MONOMER PROTEIN WITH BONE MORPHOGENETIC ACTIVITY AND MEDICINAL AGENT CONTAINING THE SAME FOR PREVENTING AND TREATING DISEASES OF CARTILAGE AND BONE

(57) Abstract

The purpose is to provide a monomer protein effective for prevention and therapeutic treatment of bone and/or cartilage diseases. Said purpose is achieved by a monomer protein having an amino acid sequence of which cysteine contributing to dimer formation of a protein belonging to TGF- β superfamily has been replaced with another amino acid. In comparison with the corresponding dimer protein, the monomer protein has a two-fold higher activity in an osteoblast cell line to induce differentiation. Other amino acids are exemplified by serine, threonine, alanine, and valine, and preferably alanine. Said protein is prepared by using *Escherichia coli*, yeast, insect cells, and mammal cells that have been transformed by a plasmid having a DNA sequence capable of expression of said monomer protein.

